IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Patent Application of:	Group Art Unit: 1651
Applicants: Binder *et al.*	Confirmation No.: 5602
Serial No.: 10/530,164	Examiner: Kim, Taeyoon
Filed: April 4, 2005	**Certificate of Electronic Filing**
Title: For Retinal Pigment Epithelial Cell Cultures on Amniotic Membrane and Transplantation	I hereby certify that the attached Response to the Office Action dated March 11, 2008 and all marked attachments are being deposited by Electronic Filing on July 8, 2008 by using the EFS – Web patent filing system and addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.
Docket No.: 34157-707.831	By: Christine Nagy

DECLARATION UNDER 37 CFR § 1.131 OF SUSANNE BINDER, M.D.

Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

I, SUSANNE BINDER, M.D., hereby declare as follows:

1. I am an inventor of the claimed subject matter of U.S. patent application number 10/530,164 ("the '164 application"), filed on April 4, 2005. The '164 application claims priority to U.S. 60/415,986, filed **October 2002**.

2. I am Professor and Chair of Ophthalmology at the Ludwig Boltzmann Institute for Retinology and Biomicroscopic Lasersurgery in Vienna, Austria. I have been conducting research in retinal disease for over 20 years and in retinal transplantation since 1998.

3. I understand that the Examiner has rejected the claims of the '164 application as allegedly being anticipated or obvious in view of Young et al. (WO 03/018040). I understand that Young et al. was filed in **August 2002** and claims priority back to **August 2001**.

4. I understand that the Examiner has rejected the claims of the '164 application as allegedly being obvious in view of Grueterich et al., *Investigative Ophthalmology & Visual Science* 43(1):63-71 (2002). Grueterich has a publication date of **January 2002**, less than a year before the priority date of U.S. 60/415,986.

5. The methods disclosed and claimed in the '164 application were conceived before August 2001.

6. Before August 2001, Dr. Scheffer Tseng and I conceived of the idea of treating a retinal disease by inserting a composite comprising amniotic membrane and confluent retinal pigment epithelial (RPE) or RPE equivalent cells on the membrane, in a subretinal space of a patient. We decided that we should set up a collaboration in this regard and developed approaches for making, testing and using these composites. Dr. Tseng and I discussed ways to develop culturing and characterization techniques using animal tissue, ways to develop an animal model of RPE atrophy or degeneration similar to age related macular degeneration, and surgical techniques to transplant the amniotic membrane and RPE cells to the subretinal space. Within a year we had a working example of these composites using the approaches developed prior to August 2001.

7. In August 2001, Boris V. Stanzel, a medical student from my laboratory, contacted Dr. Tseng with regards to performing experiments for this project. Between August and October 2001 Dr. Tseng taught Mr. Stanzel how to grow RPE cells (rabbit and human) on amniotic membrane, with intact amniotic epithelial cells or epithelially denuded. He also discussed with him creating an RPE lesion experimentally to mimic retinal disease such as age related macular degeneration and other similar diseases, and surgical transplantation of RPE on amniotic membrane to the subretinal space.

8. On or about October 2001 Mr. Stanzel began conducting preliminary experiments under my and Dr. Tseng's direction. Mr. Stanzel first isolated rabbit RPE cells and cultured them. Mr. Stanzel passaged the RPE cells once they reached confluence and then seeded the cells onto plastic, intact human amniotic membrane, and epithelially denuded human amniotic membrane.

The RPE cells were grown on these constructs until they reached confluence. These preliminary culturing experiments were conducted for several months.

9. On or about February 2002 Mr. Stanzel, under my and Dr. Tseng's direction, then began to characterize his RPE cultures both morphologically and phenotypically. Resultant epithelial phenotypes were characterized by immunostaining using antibodies. Cytokeratin 18 was used to identify the epithelial origin of RPE cells; RP 65 was used as a marker for RP differentiation, and Zo-1 was used as a marker for the tight junction complex formed by the RPE cells. The immunostaining experiments took several months.

10. By July 2002 Mr. Stanzel's preliminary data demonstrated that RPE cells could be grown on intact and denuded amniotic membrane, and that the cells were cuboidal and had a normal phenotype. Importantly, the RPE cells used in these experiments were primary cells that had been obtained from a rabbit and were not immortalized RPE cells.

11. By August 2002 Dr. Tseng and I were satisfied that the experiments Mr. Stanzel conducted verified that our inventive concept that we conceived over a year earlier worked, and that it was ready for patenting.

12. In August 2002 Dr. Tseng and I decided to file a provisional application based on the above results. The application was filed in October 2002.

13. In summary, the methods for treating retinal disease disclosed in the '164 application were conceived before August 2001, the priority date of Young et al., and before January 2002, the publication date of Grueterich et al., and steps were diligently taken to reduce the invention to practice up to the filing date of October 2002.

14. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with knowledge that willful false settlements and the like so made are punishable by fine or imprisonment, or both, under Section § 1001 of Title XVIII of the United

States Code and that willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Susanne Binder, M.D.

Date: July 8th 2009 Signature: Dr. Susanne Binder